

REMARKS

Reconsideration is requested.

In addition to the items requested in the paper filed April 17, 2009, the Examiner is requested to return an initialed copy of the previously filed PTO 1449 Form with the Examiner indicating that "International Search Report of PCT/GB2004/003273, mailed 3 November 2004" and "British Search Report dated December 23, 2003, issued in connection with GB 0318679.8" has been considered in a manner where same will be listed on the face of any patent issuing from the present application. The applicants acknowledge, with appreciation, the Examiner's indication on page 2 of the Office Action dated April 2, 2009, that the documents have been considered. The applicants note however that the Patent Office has regularly listed such documents on the face of issued U.S. Patents as notice within the issued patent of documents and information considered by the Examiner. The applicants note, for example, as evidence of the Patent Office practice in this regard, that the Patent Office has issued 102,125 patents since 1976 which contain the phrase "Search Report" as a description of documents listed under "Other References" on the face of issued patents. The following is a listing of the first 50 U.S. Patent Nos. and titles of patents obtained from a "Quick Search" of the U.S. Patent Office web site which met this criteria:

PAT. NO.	Title
1	<u>D601,242</u> T <u>Access device</u>
2	<u>D601,238</u> T <u>Filter cartridge</u>
3	<u>D601,172</u> T <u>Media device</u>
4	<u>7,596,804</u> T <u>Seamless cross-site user authentication status detection and automatic login</u>

- 5 7,596,792 T Method and system for supporting a plurality of event types
- 6 7,596,786 T Method and apparatus for utilizing an existing product code to issue a match to a predetermined location on a global network
- 7 7,596,783 T Methods and apparatus to implement annotation based thinking
- 8 7,596,767 T System and process for controlling electronic components in a ubiquitous computing environment using multimodal integration
- 9 7,596,765 T Sound feedback on menu navigation
- 10 7,596,760 T System and method for selecting a tab within a tabbed browser
- 11 7,596,752 T Delaying optimal paragraph layout during editing
- 12 7,596,730 T Test method, test system and assist board
- 13 7,596,718 T Ranged fault signatures for fault diagnosis
- 14 7,596,705 T Automatically controlling processor mode of multi-core processor
- 15 7,596,701 T Online data encryption and decryption
- 16 7,596,656 T Memory cards with end of life recovery and resizing
- 17 7,596,645 T Method for automatically adapting to the capabilities of a data-transmitting terminal and a device supplying data to said terminal requesting the data
- 18 7,596,644 T Transmit rate pacing system and method
- 19 7,596,643 T Storage subsystem with configurable buffer
- 20 7,596,637 T Storage apparatus and control method for the same, and computer program product
- 21 7,596,631 T Web browser of wireless device having serialization manager for maintaining registry of converters that convert data into format compatible with user interface of the device
- 22 7,596,627 T Methods and apparatus for network congestion control
- 23 7,596,625 T Peer-to-peer grouping interfaces and methods
- 24 7,596,622 T Apparatus and method for processing web service descriptions
- 25 7,596,614 T Network including snooping
- 26 7,596,609 T WWW addressing
- 27 7,596,593 T Methods and apparatus for efficiently transmitting interactive application data between a client and server using markup language
- 28 7,596,581 T Relevance ranking of spatially coded documents
- 29 7,596,579 T Method of reproducing an information storage medium having data structure for being reproduced adaptively according to player startup information
- 30 7,596,574 T Complex-adaptive system for providing a facted classification
- 31 7,596,571 T Ecosystem method of aggregation and search and related techniques
- 32 7,596,560 T System and method for adaptive query identification and acceleration
- 33 7,596,552 T Method and system for extracting web data
- 34 7,596,548 T Query evaluation using ancestor information

- 35 7,596,535 T Apparatus for the classification of physiological events
- 36 7,596,531 T Method and apparatus for protecting against side channel attacks against personal identification numbers
- 37 7,596,523 T Method and apparatus for network-based portfolio management and risk-analysis
- 38 7,596,522 T Computer program product for fully insuring large bank deposits
- 39 7,596,520 T Systems and methods for general aggregation of characteristics and key figures
- 40 7,596,510 T Method, system and apparatus for requesting status information from a common carrier
- 41 7,596,466 T Inclination calculation apparatus and inclination calculation program, and game apparatus and game program
- 42 7,596,463 T Method and storage medium for calibrating a holographic storage system
- 43 7,596,459 T Apparatus and methods for multi-channel electric metering
- 44 7,596,458 T Tracking vibrations in a pipeline network
- 45 7,596,444 T Vehicle skid control device, automobile with vehicle skid control device mounted thereon, and vehicle skid control method
- 46 7,596,435 T Vehicle communication system and method with mobile data collection
- 47 7,596,432 T Method for estimating the food temperature inside a refrigerator cavity and refrigerator using such method
- 48 7,596,415 T Medical devices incorporating carbon nanotube material and methods of fabricating same
- 49 7,596,408 T Implantable medical device with anti-infection agent
- 50 7,596,403 T System and method for determining path lengths through a body lumen

The applicants note that the first U.S. utility patent listed above contains the following listed reference under "Other References": "International Search Report for PCT Application Serial No. PCT/US03/21244, cited by other". The second U.S. utility patent listed above contains the following listed reference under "Other References": "Search Report issued on Jan. 13, 2004 in counterpart foreign application in GB under application No. 317110.5, cited by other."

Further, the Examiner's Supervisor, Examiner Voitach, is listed as the Primary Examiner on the following 25 issued U.S. Patents where the phrase "Search Report" is contained in the list of "Other References":

PAT. NO.	Title
1 7,393,683	<u>T Mammalian host cell modified by RNAi to inhibit .alpha. 1,6-fucosyltransferase</u>
2 7,371,375	<u>T Protein</u>
3 7,332,318	<u>T Calcium-independent phospholipases A.sub.2. genes thereof and promoter of the same</u>
4 7,329,530	<u>T Chimaeric phages</u>
5 7,312,058	<u>T Mutant serine acetyltransferase</u>
6 7,309,602	<u>T Compositions and methods for producing fermentation products and residuals</u>
7 7,285,413	<u>T Isolation tool for viable c-kit expressing cells</u>
8 7,256,016	<u>T Recycling system for manipulation of intracellular NADH availability</u>
9 7,252,943	<u>T In Vitro sorting method</u>
10 7,241,744	<u>T Treating anemia in subjects by administration of plasmids encoding growth hormone releasing hormone</u>
11 7,241,594	<u>T Gene encoding formate dehydrogenases D & E and method for preparing succinic acid using the same</u>
12 7,186,812	<u>T Isolated human G-protein coupled receptors, nucleic acid molecules encoding human GPCR proteins, and uses thereof</u>
13 7,172,893	<u>T Virus vectors and methods of making and administering the same</u>
14 7,135,613	<u>T Chimeric gene constructs for generation of fluorescent transgenic ornamental fish</u>
15 7,101,971	<u>T Erythropoietin analog-human serum albumin fusion</u>
16 7,067,714	<u>T N-calcium channel knockout animal</u>
17 7,067,308	<u>T Vector for genetically modifying non-human animals</u>
18 7,053,187	<u>T Sperm-specific monoclonal antibody, mAbC</u>
19 7,045,346	<u>T Nucleic acid constructs useful for glucose regulated production of human insulin in somatic cell lines</u>
20 6,982,362	<u>T .alpha.-tocopherol transport protein knockout animal</u>
21 6,939,711	<u>T Control of gene expression in plants by receptor mediated transactivation in the presence of a chemical ligand</u>
22 6,916,603	<u>T Methods of using agents that modulate bone formation and inhibit adipogenesis</u>
23 6,903,196	<u>T Methods for identifying and isolating tissue-specific lumen-exposed molecules</u>
24 6,891,082	<u>T Transgenic non-human animals expressing a truncated activin type II receptor</u>

25 6,878,692 **T** Apoptin-associating protein

The applicants note that the current Examiner is listed as the Primary Examiner on the following two (2) issued U.S. patents wherein the following "Search Reports" are listed on the face of the patents under "Other References":

PAT. NO.	Title
1	<u>7,468,181</u> T <u>Means and methods for the production of adenovirus vectors</u>
2	<u>7,465,583</u> T <u>Duplexed parvovirus vectors</u>

"PCT International Search Report, PCT/EP03/50125, dated Sep. 19, 2003. cited by other ." and "European Search Report, European Application No. EP 05076932.2, dated Mar. 17, 2006 (8 pages). cited by other .", respectively

Finally, the applicants note that the current Examiner is listed as the Assistant Examiner on the following two (2) issued U.S. patents wherein the following "Search Reports" are listed on the face of the patents under "Other References":

PAT. NO.	Title
1	<u>7,125,695</u> T <u>Directed evolution of microorganisms</u>
2	<u>6,635,422</u> T <u>Methods for isolating and characterizing endogenous mRNA-protein (mRNP) complexes</u>

"International Search Report for PCT/US00/13337. cited by other. " and "International Search Report for PCT/US00/35583, Apr. 18, 2001. ", respectively.

The applicants submit, with due respect, that the Patent Office has a history of listing information considered by the Examiner, including Search Reports, on the face of issued U.S. and Search Reports are not believed to be excluded under Rule 98.

Return of completely initialed PTO 1449 Forms, pursuant to MPEP § 609, is requested.

The specification has been revised in a manner suggested by the Examiner to obviate the objection to the drawings. Withdrawal of the objection to the drawings is requested.

The Examiner indicates on page 1 of the Office Action dated April 2, 2009 that none of the certified copies of the priority documents have been received. The Patent Office Image File Wrapper indicates however that a certified copy of the priority document has been received by the Patent Office. Specifically, the following "DO/EO WORKSHEET" is contained in the PTO IFW, without annotation:

DO/ EO WORKSHEET

Paralegal/ National Stage Division

U.S. Appl. No. 10/567453

International Appl. No. 480403273

Application filed by: ☐ 20 months ☒ 30 months

WIPO PUBLICATION INFORMATION:

Publication No.: WO 2005/014800

Publication Language: ☒ English ☐ German ☐ Japanese ☐ Chinese ☐ Korean
☐ French ☐ Spanish ☐ Russian ☐ Other

Publication Date: 190205

Not Published: ☐ U.S. only designated ☐ EP request

Published: ☐ LP request

INTERNATIONAL APPLICATION PAPERS IN THE APPLICATION FILE:

☒ International Application (RECORD COPY)

☐ PCT/HB/331

☐ Article 19 Amendments

☐ Request form PCT/RO/101

☒ PCT/ISPA/409 IPR: ☒ EP ☐ JP ☐ SE ☐ AU

☒ PCT/ISA/210 - Search Report: ☒ EP ☐ JP ☐ SE ☐ AU

☐ US ☐ FR ☐ CH ☐ ES ☐ RU ☐ AT ☐ KR

☐ US ☐ EP ☐ CH ☐ RS ☐ RU ☐ AT ☐ KR ☐ OTHER

☐ PCT/ISA/409 IPR was NOT AVAILABLE at the time of
patent review

☐ NONE

☐ Annexes to 409

☐ Search Report References

☒ Priority Document(s) No. 2

☒ Other: 308

RECEIPTS FROM THE APPLICANT (other than checked above):

☒ Basic National Fee (or authorization to charge)

☒ Preliminary Amendment(s) Filed on: _____

☒ Description ☒ Claims ☒ Abstract

☒ Information Disclosure Statement(s) Filed on: _____

☒ Drawing Figure(s) - (# of drwgs. 14)

☐ Assignment Document (forwarded to
Assignment Branch) 1. _____

☐ Translation of Article 19 Amendments

☐ Assignee PG Publication Notice

☐ entered ☐ not entered:

☐ Substitute Specification Filed on: _____

☐ not a page for page substitution
☐ replaced by Article 34 Amendment

☐ Annexes to 409

☒ Verified Small Status Statement 1. _____

☐ entered ☐ not entered:

☒ Oath/ Declaration (executed) 18 July 2006
☐ unsigned ☐ no citizenship

☐ not a page for page substitution
☐ no translation ☐ other: _____

☐ DNA Diskette ☐ Sequence Listing

☐ Application Data Sheet

☐ Power of Attorney/ Change of Address

☐ Other: _____

NOTES: ☐ I.A. used as Specification ☐ Other:

35 U.S.C. 371 - Receipt of Request (PTO-4398)

Date Acceptable Oath/Declaration Received

Date of Completion of requirements under 35 U.S.C. 371

Date of Completion of ALL requirements

Date of Completion of DO/EO 903 - Notification of Acceptance

Date of Completion of DO/EO 905 - Notification of Missing Requirements

Date of Completion of DO/EO 909 - Notification of Abandonment

Date of Completion of DO/EO 916 - Notification of Defective Response

Date of Completion of DO/EO 922 - Notification to Comply w/ Requirements for Patent

Applications Containing Nucleotide and/or Amino Acid Sequence Disclosures

Date of Completion of DO/EO 923

The Examiner is requested to confirm receipt of the priority documents in a further paper.

Claims 1-16, 33-41 and 43-50 are pending.

Claims 1 and 10 have been revised in a manner suggested by the Examiner to obviate the objection to same. Withdrawal of the objection to claims 1 and 10 is requested.

The Section 102 rejection of claims 1, 4-11, 14-16, 33, 34, 37-41, 43 and 46-50 over Field (U.S. Patent No. 6,593,140), is traversed. While claim 42 has been rejected over Field under Section 102, the claim was canceled, without prejudice, in the Preliminary Amendment filed February 7, 2006. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

The Examiner asserts that the medium used in example 5 was serum-free, citing example 2 as evidence. However, example 5 is silent regarding the presence or absence of serum, the media is characterized only by the presence of transferrin or tropolone with 0.2mg/l ferric ammonium citrate, or by presence of 0.2mg/l ferric ammonium citrate in the absence of transferrin or tropolone.

Field describe use of the lipophilic iron chelator tropolone (2-hydroxy-2,4,6-cycloheptatrien-1-one), particularly in agitated cell culture.

"We have now found that 2-hydroxy-2,4,6-cycloheptatrien-1-one meets all of these criteria and may be used advantageously in animal cell culture to support the growth of cells. In particular, we have found that its use can support growth in agitated cell culture, where it is necessary to use low iron concentration to avoid toxicity problems, and where

the use of other recognised chelating agents such as citrate and gluconate has failed.”

Example 5 discloses that a medium containing 0.2 mg/l ferric ammonium citrate did not support the growth of mouse myeloma cells as the myeloma cells:

“...failed to thrive and died within 48 hours”

Thus Field *et al.* (which corresponds to WO 94/02592, acknowledged in the background of the present application) do not disclose growth of mouse myeloma cells in agitated suspension culture the presence of low concentrations of iron, unless transferrin or tropolone is present.

In contrast, the present inventors have demonstrated that a medium containing low concentrations of iron is capable of supporting the growth of a myeloma cell line in methods and processes involving agitated suspension culture in the absence of transferrin or a chelator such as tropolone.

The method and process of the claims are not anticipated by Field and withdrawal of the Section 102 rejection is requested.

The Section 102 rejection of claims 1-7, 33-41 and 43-50 over Gorfien (U.S. Patent Application Publication No. 2006/0148074), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

Gorfien is derived from WO98/08934, which is acknowledged in the present specification. Gorfien discloses culture of cells in replacement media “1x medium” ¶[0137] in which animal proteins, transferrin or insulin, are replaced with ferrous sulphate chelate ¶[0137]; the preferred ferrous sulphate chelate being the nitrogen-containing chelate ferrous sulphate EDTA (¶[0113], Example 2). Use of ferric citrate in

the form of FeCl_3 -sodium citrate is mentioned but this was required at a higher concentration than the ferrous sulphate EDTA (Example 2). Gorfien disclose that low iron concentrations can be used for growth of certain mammalian cells but only when iron is present as a chelate with a nitrogen-containing chelating compound, such as EDTA. The presence of such nitrogen-containing chelators is specifically excluded from the media used in the methods and processes of the present invention.

Accordingly, Gorfien is not believed to disclose methods and processes according to the presently claimed invention. Withdrawal of the Section 102 rejection is requested.

The Section 103 rejection of claims 1-16, 33-41 and 43-50 over Field in view of Gorfien is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

Gorfien desire to produce a replacement medium free from animal proteins such as transferrin (see ¶[0032]). At ¶[0112], Gorfien state that:

"In accordance with the invention, transferrin is replaced with iron or an iron-containing compound and/or insulin is replaced with zinc or a zinc containing compound. Preferably, iron chelate compounds are used in accordance with the invention."

When culture of myeloma cells is discussed, Gorfien teach media ("1x medium", supplemented with a lipid mixture) for culturing NS/O myeloma cells (see ¶[0144]). It is stated that the "iron chelate compound" is preferably added to the 1x medium prior to filter sterilization see, e.g. ¶[0138], ¶[0141].

Thus, Gorfien teach that iron be provided in the form of an iron chelate compound as described in ¶[0113]:

" [0113] Fe^{2+} and/or Fe^{3+} chelate compounds which may be used include but are not limited to compounds containing an Fe^{2+} and/or Fe^{3+} salt and a chelator such as ethylenediaminetetraacetic acid (EDTA), ethylene glycol-bis(β -aminoethyl ether)-N,N,N',N'-tetraacetic acid (EGTA), deferoxamine mesylate, dimercaptopropanol, diethylenetriaminepentaacetic acid (DPTA), and trans-1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid (CDTA). For example, the iron chelate compound may be a ferric citrate chelate or a ferrous sulfate chelate. Preferably, the iron chelate compound used is ferrous sulphate.7H₂O EDTA ($\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ EDTA, e.g., Sigma F0518, Sigma, St. Louis, Mo.). In the medium of the present invention, the concentration of Fe^{2+} and/or Fe^{3+} can be optimized using only routine experimentation. Typically, the concentration of Fe^{2+} and/or Fe^{3+} in the 1x medium of the present invention can be about 0.00028 to 0.011 g/L. Preferably, the concentration of iron is about 0.0011 g/L."

Gorfien do not teach the use of ferric ammonium citrate.

The Examiner asserts that it would have allegedly been obvious to one of ordinary skill in the art at the time the invention was made to use ferric ammonium citrate as taught by Field in the media taught by Gorfien. The applicants respectfully disagree with the Examiner's conclusion and consideration of the following in this regard is requested.

Field is not a predictable starting point for those of ordinary skill in the art seeking to culture myeloma cells in the absence of transferrin or tropolone (a lipophilic iron chelator) as required by the present claims.

Field discloses that a medium containing 0.2 mg/l ferric ammonium citrate, in the absence of an iron chelator (transferrin or tropolone), did not support the growth of

mouse myeloma cells, as the myeloma cells: "...failed to thrive and died within 48 hours" (Example 5).

Thus, Field teaches away from use of ferric ammonium citrate in the absence of an iron chelator.

The stated aim of Gorfien is to produce a replacement medium free from animal proteins such as transferrin (see ¶[0032]). One of ordinary skill in the art combining Gorfien with the teaching of Field would have been directed, at best, to have modified the media taught by Gorfien to include ferric ammonium citrate and the lipophilic iron chelator tropolone, because Field teach that a medium containing ferric ammonium citrate does not support myeloma cell growth unless either transferrin or tropolone is present.

The methods and processes claimed require culture of myeloma cells in the absence of transferrin or a lipophilic iron chelator such as tropolone. The applicants respectfully submit therefore that the claimed invention would not have been obvious over Field and Gorfien, considered individually, or in combination.

Withdrawal of the Section 103 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

OSBORNE et al.
Appl. No. 10/567,453
Atty. Ref.: 620-412
Amendment
October 2, 2009

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: /B. J. Sadoff/
B. J. Sadoff
Reg. No. 36,663

BJS:
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100